

WHAT IS CLAIMED IS:

1. A process for the purification and isolation of bicalutamide by solution crystallization, comprising the steps of:

(i) combining crude bicalutamide and a solvent;

5 (ii) crystallizing the bicalutamide from the solvent; and

(iii) collecting the crystals of bicalutamide.

2. The process of claim 1, wherein the the crystallizing step (ii) comprises seeding the bicalutamide suspension.

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3. The process of claim 1, further comprising heating the resulting bicalutamide solution to about the boiling point of the solvent.

4. The process of claim 1, wherein the solvent is selected from the group consisting
15 of water, methanol, ethanol, DCM, toluene, PE, chloroform, hexane, 1,2-dichloroethane, diethyl ether, propanol and isopropanol.

5. The process of claim 1, wherein the solvent is selected from the group consisting of ethanol, propanol and isopropanol.

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6. A process for the purification and isolation of bicalutamide by solution crystallization, comprising the steps of:

(i) combining crude bicalutamide and a first solvent;

(ii) adding a second solvent to the crude bicalutamide-first solvent mixture;

25 (iii) crystallizing the bicalutamide from the solvents; and

(iv) collecting the crystals of bicalutamide.

7. The process of claim 6, further comprising heating the bicalutamide solution of step (i) to about the boiling point of the solvent.

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8. The process of claim 7, wherein the addition of the second solvent takes place under reflux conditions.
9. The process of claim 6, wherein the crystallizing step comprises cooling the bicalutamide solution to a temperature sufficient to bring about crystallization of bicalutamide.
10. The process of claim 9, wherein the the crystallizing step comprises seeding the bicalutamide suspension.
11. The process of claim 9, wherein the temperature sufficient to bring about crystallization of bicalutamide is about 25°C.
12. The process of claim 6, wherein the first and second solvents are the same or different.
13. The process of claim 12, wherein the first and second solvents are selected from the group consisting of water, methanol, ethanol, ethyl acetate, acetonitrile, acetone, THF, propanol, DMF, DMSO and isobutyl methyl ketone.
14. The process of claim 12, wherein the first and second solvents are selected from the group consisting of ethanol, ethyl acetate, acetone, THF, propanol, DMSO and isobutyl methyl ketone.
15. The process of claim 13, wherein the amount of the first solvent is sufficient to dissolve the crude bicalutamide.
16. The process of claim 6, wherein the second solvent is an anti-solvent.
17. The process of claim 13, wherein the first solvent: second solvent system is DMF: water.

18. The process of claim 13, wherein the amount of the first solvent is sufficient to dissolve the crude bicalutamide.

19. The process of claim 13, wherein the amount of the second solvent is added in an amount sufficient to bring about an at least partially desolubilized bicalutamide.

20. The process of claim 19, further comprising, following addition of the second solvent, adding a volume of the first solvent sufficient to dissolve the at least partially desolubilized bicalutamide.

21. The process of claim 13, wherein the first solvent is ethanol and the second solvent is water.

22. The process of claim 21, wherein the temperature sufficient to bring about crystallization of bicalutamide is about 25°C.

23. A process for the purification and isolation of bicalutamide, comprising the steps of:

(i) combining crude bicalutamide and a first solvent; wherein the first solvent is an anti-solvent;

(ii) adding a second solvent to the crude bicalutamide-first solvent mixture;

(iii) crystallizing the bicalutamide from the solvents; and

(iv) collecting the crystals of bicalutamide.

24. The process of claim 23, wherein the first solvent is selected from the group consisting of toluene, ether, chloroform, water, and methanol, and the second solvent is acetonitrile.

25. The process of claim 23, wherein the first solvent is water, and the second solvent is selected from the group consisting of acetone and THF.

26. The process of claim 23, wherein the first solvent is methanol, and the second solvent is selected from the group consisting of acetone, THF and DMF.

5 27. The process of claim 23, wherein the first solvent is ethanol, and the second solvent is selected from the group consisting of THF, DMF and isobutyl methyl ketone.

28. The process of claim 23, wherein the second solvent is added in an amount sufficient to dissolve the bicalutamide.

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29. The process of claim 23, further comprising heating the bicalutamide solution formed in step (i) to about the boiling point of the solvent.

30. The process of claim 29, wherein the addition of the second solvent takes place
15 under reflux conditions.

31. The process of claim 23, wherein the crystallizing step comprises cooling the bicalutamide solution to a temperature sufficient to bring about crystallization of bicalutamide.

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32. The process of claim 31, wherein the the crystallizing step comprises seeding the bicalutamide solution.

33. The process of claim 32, wherein the temperature sufficient to bring about
25 crystallization of bicalutamide is about 25°C.

34. A method of preparing *rac*-bicalutamide, comprising the steps of:

- (i) preparing a mixture of 5-amino-2-cyano-benzotrifluoride and butyl lithium in an organic solvent;
- 30 (ii) adding ethyl-[2-{4-fluorophenyl sulfone}]-2-hydroxy propionic acid to the mixture; and

- (iii) isolating *rac*-bicalutamide by use of the crystallization procedure of claim 1.

35. A method of preparing *rac*-bicalutamide, comprising the steps of:

- (i) preparing a mixture of 5-amino-2-cyano-benzotrifluoride and butyl lithium in an organic solvent;
- (ii) adding ethyl-[2-{4-fluorophenyl sulfone}]-2-hydroxy propionic acid to the mixture; and
- (iii) isolating *rac*-bicalutamide by use of the crystallization procedure of claim 6.

36. A method of preparing *rac*-bicalutamide, comprising the steps of:

- (i) preparing a mixture of 5-amino-2-cyano-benzotrifluoride and butyl lithium in an organic solvent;
- (ii) adding ethyl-[2-{4-fluorophenyl sulfone}]-2-hydroxy propionic acid to the mixture; and
- (iii) isolating *rac*-bicalutamide by use of the crystallization procedure of claim 23.